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Interventions for improving numerical abilities: present and future

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Abstract

Low numeracy skills have a negative impact on the employment prospects and mental and physical health of individuals, and on the economic status of countries. Clearly, this is a high priority area where efficient strategies for intervention can lead to a better outcome, especially when implemented at an early age. We discuss here present and future directions for intervention. The development of such interventions has been based on the study of numerical difficulties through methods ranging from standardized tests to behavioral measures to neuroimaging. The intervention techniques range from group-based interventions targeted at strengths and weaknesses in specific components of arithmetic, to educational computer-games, to non-invasive brain-stimulation. We discuss the principles behind each method, the current evidence, and future directions.

Keywords: Cognitive training, Developmental Dyscalculia, Electroencephalography, Magnetic Resonance Imaging, Intervention, Learning Disabilities, Noninvasive Brain Stimulation, Numerical Cognition.

Mathematical achievement is one of the foundations for a thriving society. Approximately 20% of people have low numeracy skills (EACEA/Eurydice, 2011), and depending partly on diagnostic criteria, 3-13% of people are considered to have a more serious specific disability with numbers, a condition called developmental dyscalculia (DD, for a discussion on definition see Szucs & Goswami, 2013), or mathematical learning disability (MLD) (Barbarelli, Katusic, Colligan, Weaver, & Jacobsen, 2005; Butterworth, 2010; Gross-Tsur, Manor, & Shalev, 1996). Numerical difficulties are linked to lack of progress in education, increased unemployment, reduced salary and job opportunities, and additional costs in mental and physical health (Duncan et al., 2007; Parsons & Bynner, 2005). Many of these increased risks operate over and above those associated with social and educational disadvantages in general, including those associated with literacy difficulties or lack of qualifications (Gross, Hudson, & Price, 2009; Parsons & Bynner, 2005). Furthermore, the effects of numeracy skills expand beyond the life of the individual and affect society in general (Gross, et al., 2009). The current review aims to describe the current state-of-the-art of interventions to improve numerical skills, based on cognitive, educational and neuroscientific research evidence on the nature of mathematical cognition and learning.

The componential nature of arithmetic: implications for targeted intervention

One way in which neuroscience influences education is through the application of the findings of brain-based research to guide approaches to teaching and intervention. Although such applications are still at a relatively early stage, and some are based on ‘neuromyths’ rather than solid evidence (Geake, 2008), findings from neuroscience are beginning to inform behavioral and cognitive interventions (Blakemore & Frith, 2005; Goswami, 2006). We will focus here on the componential nature of arithmetic. The most striking evidence for the functional separability of different components comes from neuropsychological studies of acquired dyscalculia (Cappelletti, Butterworth, & Kopelman, 2012; Delazer, 2003; Demeyere,

Rotshtein, & Humphreys, 2012). Functional brain imaging techniques provide converging evidence that different components of arithmetic can involve different brain areas and networks (Zamarian, Ischebeck, & Delazer, 2009).

The componential nature of arithmetic is important in planning and formulating interventions with children with arithmetical difficulties. Interventions that focus on the particular components with which an individual child has difficulty are likely to be more effective than those which assume that all children's arithmetical difficulties are similar.

Systematic development of targeted programmes for children with mathematical difficulties began only recently (Torgerson et al., 2011; Wright, Martland, & Stafford, 2006). These programmes are highly intensive, and involve approximately 30 minutes of individualized intervention per day. They are generally targeted at children with severe difficulties: approximately the lowest-achieving 5%. However, they exclude many children with less severe numeracy difficulties that may nevertheless have a serious practical impact on their lives but for whom intensive intervention may not be a practical or cost-effective possibility.

In contrast, Catch Up Numeracy is an intervention based on the 'Numeracy Recovery' scheme (Dowker, 2005), which applies to primary school children with moderate mathematical weaknesses. It is a less intensive, but still highly targeted, intervention (Dowker & Sigley, 2010; Holmes & Dowker, in press) (**Box 1**).

The results so far indicate that participants who received the Catch Up intervention improved more than twice as much in Number Age on a standardized test as expected from passage of time, and made significantly higher ratio gains than controls who received non-targeted mathematical intervention (**Figure 1**). Thus, a behavioral-targeted intervention programme based on cognitive and neuroscientific principles of the targeted cognitive ability can lead to successful improvement.

In the next section we will discuss the application of neuroimaging to assess the effect of intervention on the neural substrates of atypical numeracy.

The effect of intervention on atypical neural responsiveness

Children with MLD or DD are exhibiting behavioral impairments as well as atypical brain activity and anatomy (Kucian, Kaufmann, & Von Aster, in press) (**Figure 2**). In this section we will discuss how intervention administered in a game-like fashion (**Box 2**) can affect behavior as well as brain functions. We will offer examples both from electroencephalography (EEG) and functional magnetic resonance imaging (fMRI), which provides good temporal and spatial resolution as to where activation occurs in the brain, respectively (**Box 3**).

Neural underpinnings and intervention using EEG

Electrophysiological investigations into basic numerical abilities typically focus on late parietal positivities (positive-going deflections in the P2 and P3 time window) that are assumed to be reflections of quantity-processing functions in infants, children, and adults (Dehaene, 1996; Hyde & Spelke, 2011, 2012; Izard, Dehaene-Lambertz, & Dehaene, 2008). For instance, during numerical comparison tasks larger amplitudes of the late parietal event-related potentials (ERPs) were found in response to large compared to small numerical distances (e.g., comparing the numbers 2 and 8 vs. the numbers 2 and 3), both in adults (Paulsen, Woldorff, & Brannon, 2010; Turconi, Jemel, Rossion, & Seron, 2004) and in younger populations (Heine, Tamm, Wißmann, & Jacobs, 2011; Soltész, Szűcs, Dékány, Márkus, & Csépe, 2007; Temple & Posner, 1998; but cf. Hyde & Spelke, 2009; Libertus, Woldorff, & Brannon, 2007).

Previous studies have reported atypical distance-related modulations of these late positive-going ERP components in adolescents with DD (Soltész, et al., 2007) and in children with MLD (Heine et al., 2012) during numerical comparison tasks, when compared to age-matched typical achievers. The amplitudes of the late posterior positivities are commonly assumed to be related to neural activity primarily in inferior parietal regions (e.g., Dehaene,

1996; Heine, et al., 2011; Soltész, et al., 2007), which have been suggested to play a causal role in numeracy (Cohen Kadosh et al., 2007).

Using ERP measures and standardized diagnostic measures to assess the effects of remedial training for elementary school children with MLD, a recent intervention study focused on training-related changes in groups of second and third graders (Wißmann, Heine, Handl, & Jacobs, 2013). The training was based on a highly effective intervention in third-grade children with DD (Kaufmann, Handl, & Thöny, 2003). The intervention program is theory-based, organized into semi-hierarchical modules, and focuses on the explicit teaching of basic numerical skills (e.g., semantic number knowledge) and arithmetic conceptual knowledge (e.g., understanding of arithmetic operations and principles). Over a 9-months period training sessions were offered once a week for groups of 2-6 children with each session lasting about 90 minutes.

Analysis of the data from groups of children with MLD who either took part in the numeracy intervention (intervention group) or underwent a reading and spelling training (low achieving controls), and a third group of age-matched typical achievers, revealed changes that reflect gains on typically achieving peers in diagnostic measures (Wißmann, et al., 2013), as well as electrophysiological and behavioural parameters for the intervention group (**Figure 3**). Adopting a well-documented experimental design for the EEG part of the study (Barth et al., 2006), the children were presented with symbolic and nonsymbolic approximate addition tasks before (t1) and after (t2) the intervention phase. At t1, the typical achievers showed significantly larger amplitudes of the critical ERP components than both groups of low achieving children, which is consistent with the results of previous electrophysiological studies (Heine, et al., 2012). However, the group of children who took part in the numeracy intervention program showed a marked shift in the amplitudes of the late positive-going waveform (**Figure 3**, Wißmann, Heine, & Jacobs, 2012). This suggests that the intervention did not only affect children's behavioral performances as assessed by standardized diagnostic

tools (Wißmann, et al., 2013), but changes on the behavioural level were accompanied by differences in brain functioning as assessed by EEG-measures. However, since ERPs lack the necessary spatial resolution, it is unclear whether the effects can be related to improvement in brain regions that were initially impaired, or whether other brain regions have been recruited to compensate for atypical brain organisation.

Neural underpinnings and intervention using fMRI

In the last few years a clearer picture has emerged of functional processes in the typical adult and child brain during number processing and calculation, by means of contemporary brain imaging techniques (**Box 3**). However, only a small number of imaging studies have addressed the question of neural correlates of atypical development in DD. Nevertheless, a recent meta-analysis has emphasized the neural aspects of DD (Kaufmann, Wood, Rubinsten, & Henik, 2011). Convergent evidence suggests that differences are found primarily in the intraparietal sulcus (IPS) and the superior and inferior parietal lobule, which are known to be core regions for numerical and mathematical processing. However, aside from parietal areas, other cortical and subcortical regions that contribute to numerical cognition can also be associated with mathematical difficulties. Such results include reduced brain activation found by fMRI (Kucian et al., 2006; Mussolin et al., 2010; Price, Holloway, Räsänen, Vesterinen, & Ansari, 2007) or EEG (Heine, et al., 2012; Soltész, et al., 2007) and atypical brain metabolism by magnetic resonance spectroscopy (MRS) (Levy, Reis, & Grafman, 1999), as well as reduced grey matter volume or deficient fibre connections measured by morphometric MRI (Rotzer et al., 2008) and diffusion tensor imaging (DTI) (Rykhlevskaia, Uddin, Kondos, & Menon, 2009). Moreover, compensatory mechanisms have been observed in DD children; these are usually characterized by stronger recruitment of supporting areas associated with working memory, attention, monitoring, updating or finger representation (Kaufmann et al., 2009; Kucian, Loenneker, Martin, & von Aster, 2011). Such an increased need for additional supportive functions might be explained by underdevelopment of number representations,

and/or a failure in automatization of access to these representations. Aberrant brain activation, structure or metabolism in children with DD has not yet been integrated into the diagnose, but studies in the field of ADHD and reading pointed to the promising potential of combining behavioural measures with neuroimaging markers to improve diagnostic accuracy or to predict further outcome (Brem et al., 2012; Brown et al., 2012; Sidhu, Asgarian, Greiner, & Brown, 2012).

However, the human brain is a highly plastic organ and adequate stimulation is able to induce structural as well as functional changes. A 5-weeks computer-based intervention “Rescue Calcularis” was developed with the aim of improving number representations and strengthening the links between numbers and spatial processes on the internal mental number line (Kucian et al., 2011). Results have indicated that children with and without DD improved their spatial number representations and arithmetical abilities. This highlights the importance of a precise mapping of, and automated access to, the mental number line for adequate development of calculation skills.

Additionally, the training resulted in a modulation of brain functions. FMRI depicted a reduction in the recruitment of relevant brain regions after the training, including mainly frontal areas, bilateral IPS and the left fusiform gyrus. A decrease of brain activation in these regions and particularly of the frontal lobe is assumed to reflect automatization of cognitive processes necessary for mathematical reasoning (Zamarian, et al., 2009). In a follow-up examination 5 weeks after training, a significant increase of activity in parietal areas was found in children with DD. Since the IPS is known to play a pivotal role in number representation, these results suggested that time for consolidation after training was needed to establish neuronal representation (Kucian, Grond, et al., 2011).

In conclusion, domain-specific game-like interventions are associated with neuroplasticity in functional circuitry that is impaired in children with DD and MLD, and furthermore, they can

transform brain activation that is atypical in respect to time and localisation, into typical brain activation.

Using Transcranial Electrical Stimulation to Improve Cognitive Training

So far, we have discussed the effect of intervention on behavior and brain functions.

Intervention, by itself, aims to affect brain mechanisms by influencing cognitive functions, leading to a virtuous circle whereby these changes in brain functions also impact subsequent cognitive functions. However, transcranial electrical stimulation (TES) can have a more direct influence on brain functions and neuroplasticity (Cohen Kadosh, 2013; Krause & Cohen Kadosh, in press) (**Box 4**).

TES delivers weak electrical currents (e.g., 1-2 mA) via electrodes, most frequently at the size of 25-35cm², which are placed on the scalp above the brain area that the experimenter is interested in affecting. When the current is applied over a short duration (~20 min), it passes painlessly through the scalp and skull and alters spontaneous neural activity (Fritsch et al., 2010; Nitsche et al., 2008).

The recent results obtained from TES experiments offer promising possibilities for both the cognitive enhancement of normal abilities and treatment of impairments in different domains including attention, working memory, numeracy, language, and executive functions (for reviews see, Cohen Kadosh, 2013; Jacobson, Koslowsky, & Lavidor, 2012; Krause & Cohen Kadosh, in press).

In the numerical domain, TES positively impacted basic numerical skills, arithmetic training, symbolic learning, and automaticity (Cohen Kadosh, Soskic, Iuculano, Kanai, & Walsh, 2010; Iuculano & Cohen Kadosh, 2013; Snowball et al., in press). Notably, some of these studies have found long-lasting behavioural effects (Cohen Kadosh, et al., 2010), including transfer effect to non-learned material, and long-lasting efficiency in brain functions in the stimulated brain region (Snowball, et al., in press) that span 6 months.

Results so far have indicated that stimulation needs to be paired with cognitive training intervention and that the timing of stimulation with respect to task performance has important effects (Stagg et al., 2011). In this regard, when the aim is to improve learning, TES during intervention yields the most robust results (Reis & Fritsch, 2011; Stagg, Jayaram, et al., 2011).

TES is a portable, painless, non-invasive and inexpensive method. These characteristics increase the likelihood of future use of TES in different populations outside of the laboratory, in clinics or in educational institutions (Krause & Cohen Kadosh, in press). However, currently there is only a limited amount of work with paediatric populations (Krause & Cohen Kadosh, in press), which leaves questions as to its safety and efficacy, as well as to the possible mental cost of cognitive enhancement (Iuculano & Cohen Kadosh, 2013) in this population.

Summary

In this review, we discussed recent approaches to intervention such as targeted intervention and computer-based intervention, as well as the effect of intervention on brain functions, and the possibility in the future in enhancing cognitive training intervention using TES. These approaches and their possible combinations (**Figure 4**) serve as an excellent example for the fruitful synergy among the fields of psychology, neuroscience, and education; together, these disciplines can contribute to optimal designs for intervention targeting neurocognitive mechanisms, and can furthermore evaluate the efficacy of such interventions at the behavioral and brain levels. As with any new development, some of the interventions are still at an early stage. E.g., some studies might have involved relatively small, non-random samples, or did not include control groups (see **Table 1** for a summary of the studies in this review).

However, as we described here there is increasing evidence for the effectiveness, in the short- and even long-term, of some interventions, including transfer effect to non-trained material

(**Table 1**) that is sometimes lacking in interventions (**Box 5**). While much work is still needed and outstanding questions need to be answered (**Box 5**), the current review provides an example of the potential for improving and optimising intervention for learning difficulties.

Box 1. Catch Up Numeracy

Children in the project receive interventions from trained teachers or teaching assistants during two 15 minute sessions per week, typically for one school term.

The components are as follows:

- (1) Counting verbally (counting verbally from 0 or 1; counting on from a given number; counting back from a given number)
- (2) Counting objects (counting objects; order irrelevance; repeated addition of objects; repeated subtraction of objects)
- (3) Reading and writing numerals and number words
- 4) Handling tens and units (number comparison; adding tens and units; subtracting tens and units).
- (5) Ordinal numbers (stating the ordinal position – e.g. second, fourth, etc – of a bead within a bead string)
- (6) Word problems.
- (7) Translation between different formats (i.e. between quantities of objects and number words or numerals),
- (8) Derived fact strategies (including the use of commutativity of addition and the inversion principle for addition and subtraction to derive unknown number facts from a given number fact).
- (9) Estimation of set size, and of answers to arithmetic problems.
- (10) Remembered number facts.

Each child is assessed individually by a trained teacher/teaching assistant using ‘Catch Up Numeracy formative assessments’ which the member of staff then uses to complete the ‘Catch Up Numeracy learner profile’. This personalised profile is used to determine the entry level for each of ten Catch Up Numeracy components and the appropriate focus for numeracy teaching. Children are provided with mathematical games and activities targeted to their

specific levels in specific activities. Where possible, these games and activities involve the use of materials that are commonly available in schools.

Each 15-minute teaching session includes (i) a review and introduction to remind the child of what was achieved in the previous session and to outline the focus of the current session; (ii) a numeracy activity; and (iii) a linked recording activity where the child records the results of the activity in oral, written, and/or concrete fashion, and where the child receives focused teaching related to their performance in the activity and to any observed error.

Box 2. Computer-based interventions

As the development of each child's numerical abilities follows different trajectories and is intertwined with the development of other cognitive domains, a high grade of individualization is needed. Adaptive educational computer-based training can contribute to these requirements. Computer-based intervention can be designed to adapt for cognitive or performance profiles and provides intensive training in a stimulating environment. In combination with the fact that the computer is an emotionally neutral medium, it may also foster motivation and enhance positive self-concepts as every child gains feelings of success (Ashcraft & Faust, 1994; Spitzer, 2009). Moreover, computers are an attractive medium for children and seem to be effective when trainings are sensibly constructed (Fletcher-Flinn & Gravatt, 1995; Kulik, 1994). However, it has to be kept in mind that computers cannot replace teachers or therapists, but interactive games can form helpful tools for successful remediation. Regarding the math intervention, only a few computer-based trainings have been evaluated scientifically:

The training called "Number Race" is based on principles for remediation of DD and focuses on quantity representation and the association between number and space (Wilson et al., 2006). Evaluation indicated a significant improvement in basic numerical cognition, but the effect did not generalize to counting or arithmetic (Räsänen, Salminen, Wilson, Aunio, & Dehaene, 2009; Wilson, Dehaene, Dubois, & Fayol, 2009; Wilson, Revkin, Cohen, Cohen, & Dehaene, 2006).

"Elfe and Mathis I" is a recently developed computer-based program which trains basic numeric capabilities, arithmetic and geometry (Lenhard, Lenhard, Schug, & Kowalski, 2011). The program is aligned to the school curriculum and its evaluation demonstrated a higher increase in mathematical competence in the training group compared to matched controls.

Another computer-assisted instruction (CAI) to enhance number combination skills has been presented by Fuchs et al. (2006). The training was effective in improving addition but not subtraction, and no transfer to arithmetic story problems occurred.

Finally, the training, “Rescue Calcularis,” discussed in the text, has been further developed.

The new extended version is called “Calcularis” and includes a variety of games designed in line with current neurocognitive concepts of mathematical development, insights on DD and general learning principles (Käser et al., 2012; Käser et al., 2011). The innovation of Calcularis is the use of an adaptive control algorithm which enables individual adjustment on the difficulty level as well as the choice of appropriate games. Evaluation showed that children benefited from the training regarding number representation, and addition and subtraction skills (von Aster, Käser, Kucian, & Gross, 2012).

Box 3. Brain imaging methods

Cognitive neuroscience combines strategies of cognitive psychology with different methods to examine brain structure or brain function. Thanks to these modern brain imaging techniques, we are able to generate high resolution anatomical images of our brains, examine fibre tracts, gain metabolic insights, or observe brain activation while we are performing a task.

Magnetic resonance imaging (MRI)

MRI produces brain images non-invasively by a powerful magnet and radio-frequency. Different MRI acquisition methods provide information about various aspects of our brains. The recording of high resolution anatomical brain images allows to differentiate between grey and white brain matter and to investigate focal differences in morphometry. Alternatively, DTI enables the measurement of the integrity of fibre connections between different brain regions and MRS measures brain chemistry to study changes of various brain metabolites. Finally, fMRI uses the change in oxygen levels of the blood in active brain areas to create images of brain regions that are active during a specific task.

Positron emission tomography (PET)

PET-imaging enables the visualization of biochemical and physiological functions of the brain. A radioactive tracer is injected into the blood system. Areas of high radioactivity indicate high amounts of radioactive-labelled oxygen, and therefore are associated with brain activity; similar to the principle of fMRI, it is assumed that active regions are flooded with oxygenated blood.

Near infrared spectroscopy (NIRS)

1 Near infrared light is shined through the head, travels through the outer layers of the brain,
2 and is measured by a nearby receiver as it leaves the head. By measuring the quantity of
3
4 returning photons, one can infer the spectral absorption of the underlying tissue and make
5
6 some conclusions about its average oxygenation and deoxygenation. Therefore, NIRS can be
7
8 used for non-invasive assessment of brain function by detecting changes in oxygen
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10 concentrations in the blood which are associated with neural activity.
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16 *Electroencephalography (EEG) / Magnetoencephalography (MEG)*

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19 Electrophysiological methods register the electrical activity of neurons non-invasively.
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21 Depolarisations of synchronously active neurons create electrical and magnetic fields that can
22
23 be recorded at the scalp. While EEG measures the changes of the electric field with electrodes
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25 placed on the scalp, MEG records magnetic field changes by an arrangement of
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27 superconductive coils. In contrast to fMRI and PET, which provide high spatial resolution but
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29 lower temporal resolution, electrophysiological methods measure across larger regions of the
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31 brain but can detect changes of brain activation in the millisecond-range.
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Box 4. Types and Mechanisms of Transcranial Electrical Stimulation

Transcranial direct current stimulation (TDCS) involves the application of a constant electrical current. Studies on animals and humans have found that the induced changes in tissue excitability vary with current polarity. Anodal stimulation pushes neural resting membrane potentials closer to the activation threshold and therefore increases tissue excitability, while the reverse polarity, cathodal stimulation, inhibits cell firing and decreases excitability (Fritsch, et al., 2010; Nitsche & Paulus, 2000). Most of the studies so far found that anodal stimulation improved human performance, while cathodal stimulation impaired human performance (Cohen Kadosh, 2013; Jacobson, et al., 2012).

The long-lasting effects of TDCS are protein synthesis-dependent and are accompanied by several mechanisms including the modifications of intracellular cyclic adenosine monophosphate (cAMP) and calcium levels (Hattori, Moriwaki, & Hori, 1990), brain-derived neurotrophic factor (Fritsch, et al., 2010), and activation of adenosine A1 receptors (Márquez-Ruiz et al., 2012) and therefore share some features with long-term potentiation and long-term depression (Castillo, Chiu, & Carroll, 2011; Neves, Cooke, & Bliss, 2008). FMRI experiments in humans have found that TDCS can alter local and remote brain activation (Holland et al., 2011; Keeser et al., 2011). MRS studies found change the local concentration of GABA and glutamate (Stagg et al., 2009), which are critically involved in learning and memory (Stagg, Bachtiar, & Johansen-Berg, 2011).

Transcranial random noise stimulation (TRNS) typically involves the generation of random ‘samples’ of alternating electrical current at a rate of several hundred times per second. These samples are randomly assigned current amplitudes, which are normally distributed around a direct-current component of 0. The random fluctuation of these sample currents between positive and negative amplitudes generates the electrical ‘noise’ that cortical regions of interest are exposed to. The technique is preferred over TDCS for its higher cutaneous perception threshold (Ambrus, Paulus, & Antal, 2010), making it easier to maintain

experimental blinds, and for its oscillatory rather than direct current, which ensures that application is independent of polarity (i.e. anodal and cathodal) (Chaieb et al., 2009).

Although the mechanisms underlying TRNS are less well-studied than TDCS, and have been attributed both to stochastic resonance or the induction of sodium ion influxes (Terney, Chaieb, Moliadze, Antal, & Paulus, 2008), this technique has been shown to enhance cortical excitability. The effect of TRNS has been suggested to be facilitatory at both electrodes. Moreover, compared to anodal TDCS, high-frequency TRNS (100-640 Hz) yields more powerful results (Fertonani, Pirulli, & Miniussi, 2011).

Box 5. Outstanding Questions

1. Might the intense intervention and great emphasis on improving a given cognitive ability have a positive effect on other mental faculties as well? It seems plausible that a positive learning experience has the potential to improve general attitudes towards learning by enhanced confidence and motivation. However, could an intense intervention have also a negative effect on a non-trained ability? The latter might occur due to a shift of metabolic consumption and neurochemical modulation caused by the intervention, which changes the respective involvement of different brain areas.
2. What are the long-term effects of the intervention programs? Do the students maintain the level displayed at post-intervention assessments, do they improve even further improve, or do they show a decline in performance? May the degree of such a decline, if one occurred, be affected by the type of intervention (e.g., computer-based vs. personal tutorials), or is it more linked to individual characteristics? Will TES be able to elongate and maintain the positive effect of intervention?
3. What are the cognitive and biological mechanisms that make computer-based cognitive training a successful tool for intervention? For example, might the attractiveness, engagement and reward-based nature of this training act on the dopaminergic system that is involved in plasticity (Lisman, Grace, & Duzel, 2011)?
4. What is the temporal dynamic between behavioral and brain changes due to intervention? Do behavioral changes precede changes in physiology or the other way around?
5. Intervention efficacy: Which socio-emotional, cognitive, neural or genetic modulating factors may affect intervention efficacy? How is the efficacy of cognitive intervention and TES in children and adults influenced by factors such as age, individual differences in cognitive abilities (Tseng et al., 2012), or level of education (Berryhill & Jones, 2012), and specific genes (Antal et al., 2010)?

6. Which intervention methods (cognitive, neuronal stimulation, etc.) and which combination of methods are most apt to exert positive intervention effects? Moreover, sometimes interventions improve performance on a specific task, but do not transfer to similar tasks (Räsänen, et al., 2009). Can these methods or their combination increase the likelihood for a transfer effect? Is there a systematic relation between intervention efficacy, neural changes and severity of mathematical difficulty?

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Table 1. Overview of the different interventions described in the current review, including sample size, age, length of the intervention, and effect sizes. Note that in the case of effect size it is not accurate to compare the different interventions, as the different interventions involved different populations, age, effects, and the intervention length varied. The reader is referred to Ise, et al., (2012) for a meta-analysis which includes other types of training not discussed here. N/A notes the inability to conclude whether the intervention enabled the individuals to improve their performance and thus catch up with their peers.

Figure 1. The effect of the Catch Up intervention program. In this study (Holmes & Dowker (in press)), 395 children received the Catch Up intervention program, which was based on the ‘Numeracy Recovery’ scheme (Dowker, 2005) in collaboration with Catch Up® (a not-for-profit UK charity). There were two smaller control groups: 1) Matched-time individualized mathematics intervention group (n=50). This group involved reviewing work done in the school lessons and was not specifically targeted to assessed individual strengths and weaknesses. 2) No intervention group, except for the usual school instruction (n=48). All children were given a number screening test before and after the intervention. At the start, participants’ mean age was 104.97 months (SD=13.6). Their mean mathematics age (mathematical achievements based on their age) was 96.46 months (SD=14.66). The groups did not differ in chronological age, or in mathematics age ($p>0.35$). The children who received the Catch Up intervention made significantly higher ratio gains (months gained in mathematics age divided by the number of months between initial and final testing) than either of the other groups as indicated by a significant effect of group ($F(2,490)=14.67$; $p<0.001$), and post-hoc tests. A detailed account of the programme and of an evaluation of its effectiveness is given by Holmes & Dowker (in press).

Figure 2. Summary of deficient brain function (pink circles), grey matter (green squares), white matter (yellow stars), and brain metabolism (blue triangle) in children with DD. Reported deficits include a variety of brain regions, however, there seems to be consistent evidence that DD is associated with deficits in the parietal lobes (marked in white) which host core regions for numerical understanding. (Brain templates by P.J. Lynch and C.C. Jaffe). Reproduced from Kucian, K., Kaufmann, L., & Von Aster, M. (in press). Brain Correlates of Numerical Disabilities. In R. Cohen Kadosh & A. Dowker (Eds.), *The Oxford Handbook of Numerical Cognition*: Oxford University Press, with permission from Oxford University Press.

Figure 3. Panel (a) gives an overview of stimulus-locked ERPs at recording site P8 for the three groups of children [intervention group: blue; typical achievers: black; low achieving controls: grey]. Pre- [solid lines] and post-results [dashed lines] are plotted for the mean grand averages over both experimental conditions, i.e., the nonsymbolic and symbolic approximate calculation tasks. The relevant ERP component is highlighted, and the topography of mean difference potentials is shown for the critical time window and contrast (i.e. typical achievers minus intervention group at t1). Panel (b) specifies diagnostic [bluish bars, with higher values indicating better performance levels; (Kaufmann, Graf, Krinzing, Delazer, & Willmes, 2008)], behavioral [greenish bars; error rates in %] and ERP parameters [reddish bars; mean amplitudes in μV , 300-500 ms after stimulus onset] for both points in time [t1, t2]. Asterisks denote Bonferroni-corrected levels of statistical significance of differences between pre- and post-testing results.

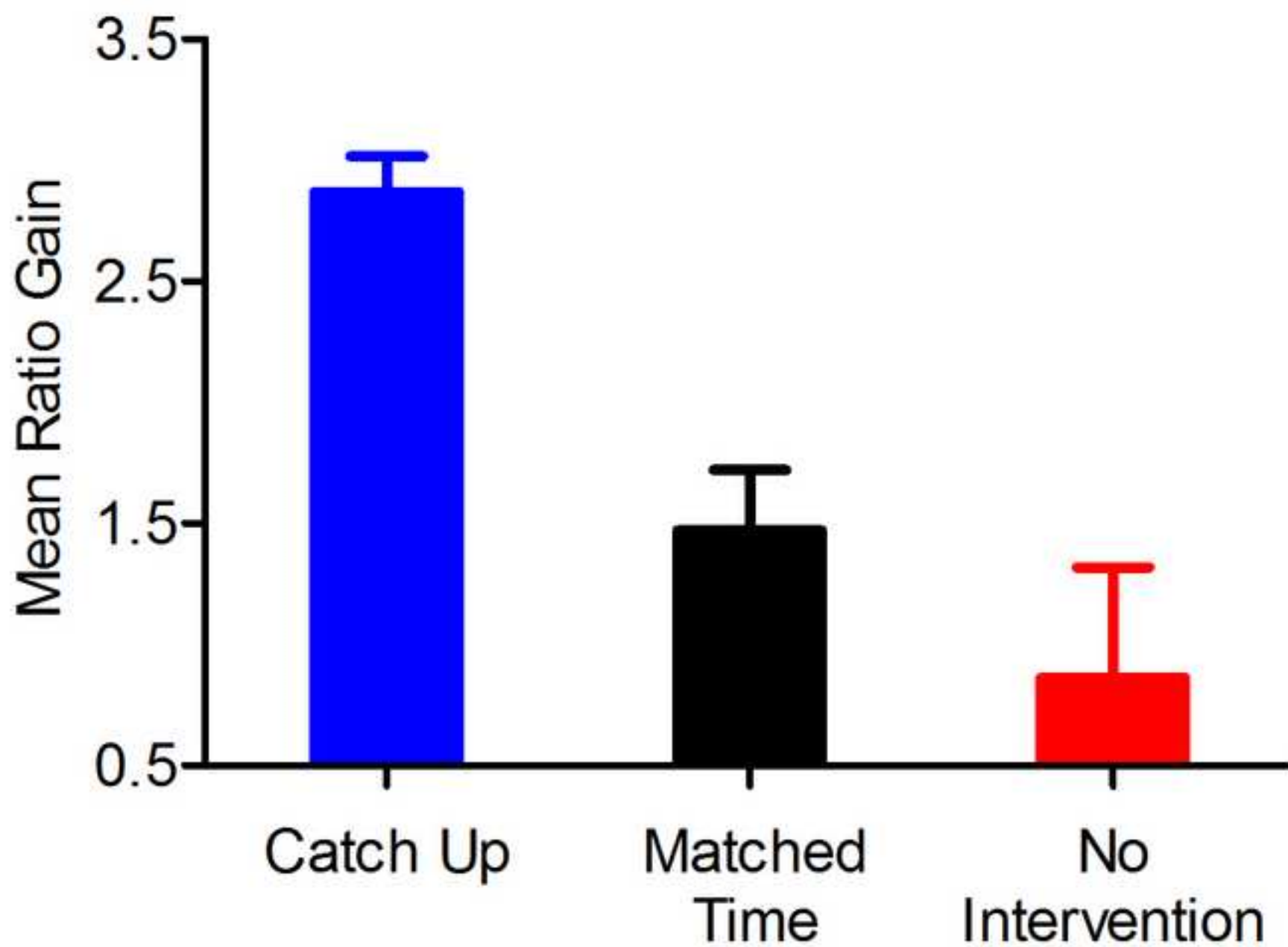
Figure 4. Combination of wireless TES and cognitive training using a video-game. In this example, a participant receives stimulation to the dorsolateral prefrontal cortex while being trained on fractions. In this training the fractions need to be mapped on a horizontal line (cf. Kucian, Grond, et al., 2011) by moving her body to the respective location between two anchors (zero and one). Body movements are detected using a motion-detector sensor (Moeller et al., 2012).

Table

Type of intervention	Sampe size	Age (in years)	Length of intervention	Country	Randomisation	Single-blind	Double-blind	Control group	Transfer effect	Catching up the difference with peers	Effect size (Cohen d')
Catch Up Numeracy educational intervention for children (Dowker & Sigley (2010); Holmes & Dowker (in press, 2013)	n = 440 (into 3 groups)	6-10	4 months	UK	No	Yes	No	Yes	Yes	Yes	Number Age gain: d = 0.47 (Intervention vs Matched Time Control; d = 0.55 (Intervention vs No-Intervention Control)
Remedial training for children with dyscalculia (Wißmann et al., 2013)	n=64 (into 5 groups)	7-11	9 months	Germany	No	Yes	No	Yes	Yes		Arithmetic skills (<i>HRT 1-4</i> ; Haffner et al., 2005): d=0.84; Visuo-spatial skills (<i>HRT 1-4</i> ; Haffner et al., 2005): d=0.63
Rescue Calcularis (Kucian et al. 2011)	n=32 (into 3 groups)	8-11	5 weeks	Switzerland	Yes	No	No	Yes, but only for children with dyscalculia	Yes	in linearity and variability of arabic digit representation	positive effects of training (pre vs post) on: Number line task: dyscalculics d=1.08, controls d=1.15; Addition & Subtraction: dyscalculics d=0.36, controls d=0.47
Calcularis (von Aster et al. 2012)	n=32 (into 2 groups)	8-11	6 weeks	Switzerland	Yes	No	No	Yes	Yes	N/A	positive effects of Calcularis vs control group: Addition d=0.31; Subtraction d=0.39; Number line task 0-10: d=0.28; 0-100: d=0.18; 0-1000: 0.15; Estimation d=0.29; Subitizing d=0.08; Heidelberger Rechentest (Haffner et al., 2005): Addition d=0.16; Subtraction d=0.52
Number Race (Wilson et al. 2006; 2009)	n=9 (into 1 group)	7-9	10 weeks	France	No	No	No	No	No	N/A	positive effects of training (pre vs post) on: large addition problems d=0.33; negative effects of training (pre vs post) on: small addition problems d=1.59
Elfe and Mathis I (Lenhard et al. 2011)	n=130 (into 4 groups)	7-9	10 weeks	Germany	No	No	No	Yes	N/A	N/A	Math skills: d=0.59 1st graders; d=0.62 2nd graders
CAI (Fuchs et al. 2006)	n=33 (into 2 groups)	1st graders	18 weeks	USA	Yes	No	No	Yes	No	N/A	positive effects of CAI vs spelling training: Addition d=0.49; Subtraction d=0.02; negative effects of CAI vs spelling training: Story problem d=0.06
TES (Cohen Kadosh, et al., 2010)	n=15 (into 3 groups)	20-22	6 days	UK	Yes	Yes	No	Yes	No	N/A	Numerical automaticity: d=1.09
TES (Iuculano & Cohen Kadosh, 2013)	n=19 (into 3 groups)	20-31	6 days	UK	Yes	Yes	No	Yes	No	N/A	Learning rate: d=0.85; Numerical automaticity: d=0.55
TES (Snowball, et al., in press)	n=51 (into 4 groups)	18-28	5 days	UK	Yes	Yes	Yes	Yes	Yes	N/A	Learning rate: d=0.89 (drill learning), 0.77 (calculation learning);

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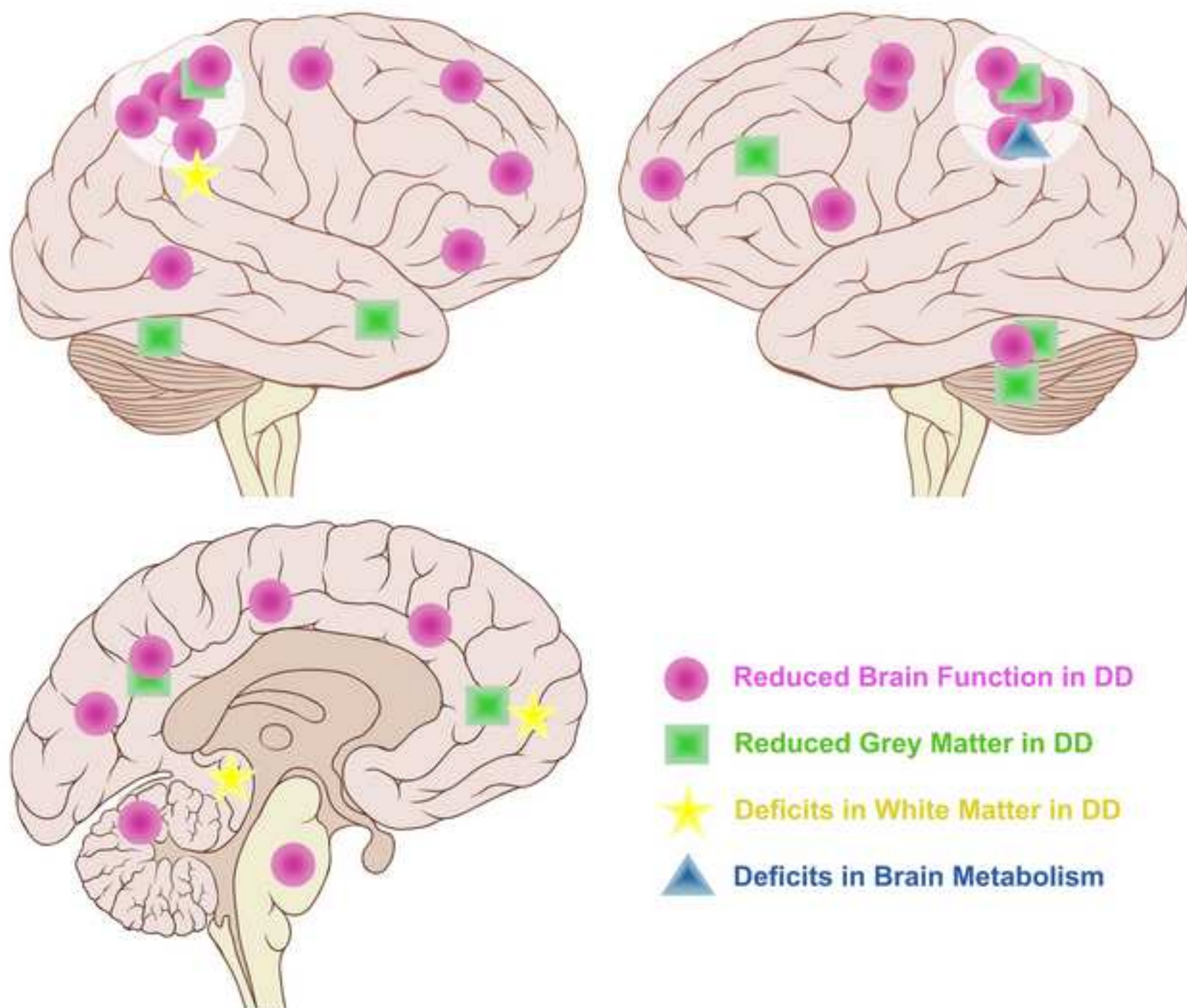
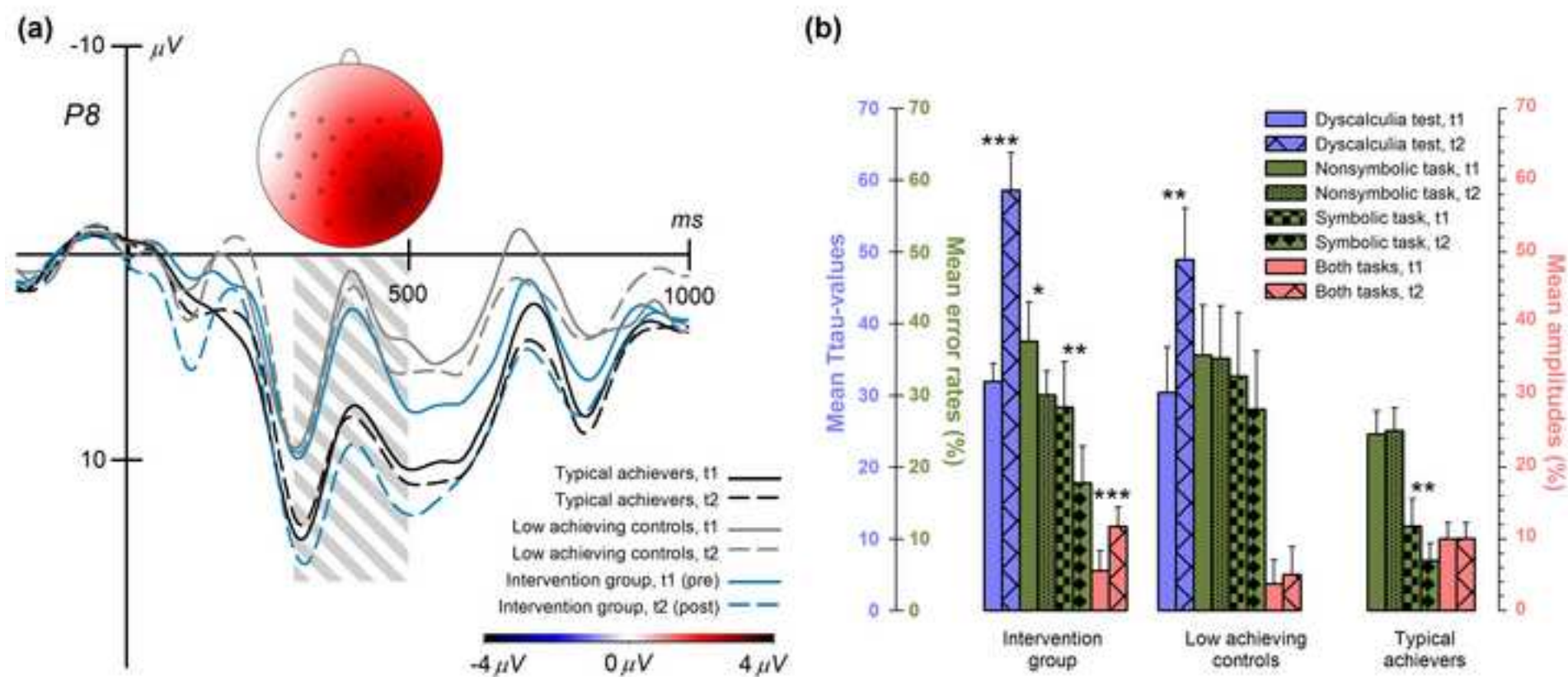


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